equivalent amount of other alcoholic beverage for periods of three days during these months. Measures should also be taken to prevent overcrowding, so far as is possible, from the middle of August to the end of December.

One might ask how soon after discharge from hospital can a patient take alcohol or resume arsenic or gold therapy? We have come across cases in which a considerable amount of alcohol was taken a few weeks after discharge without any untoward effect. We know at least one patient who received a complete course of arsenic injections after an interval of only five weeks from the date of discharge without any toxic manifestation. It should be remembered that the normal liver can withstand large doses of all these drugs. The capacity of a damaged liver depends upon the amount of damage already done. Recovery is complete in a short time in mild cases, whereas in severe cases it may be months before the liver is capable of withstanding even small doses of these drugs. In a case of moderate severity a period of six months is a reasonable interval, after which the administration of these drugs can be resumed with safety. Great caution and longer intervals are needed in relapse cases. Evidence is accumulating to support the view that a weak liver poison such as alcohol may have a stimulant action on the fibrous tissue stroma of the liver while exerting a degenerative effect on the liver parenchyma, and the prolonged stimulant action may lead to cirrhosis in course of time. In all probability these properties of the drug hold good only if the liver is already damaged by a previous attack of hepatitis, with or without jaundice. If the stroma is as much damaged as the parenchyma, stimulation can produce no proliferation, and cirrhosis is unlikely in cases of moderate or severe jaundice except as replacement fibrosis in multiple nodular hyperplasia. This is rather speculative, but it is hoped that future work will confirm it.

Summary

A review is given of 450 cases of infective hepatitis treated in a general hospital in Malta. The epidemiology, clinical types, signs, symptoms, diagnosis, complications, and cause of relapse are discussed. The effect of liver poisons—alcohol, arsenic, and gold—is described. The pathogenesis of catarrhal jaundice is reviewed critically.

The clinical findings suggest that the jaundice is partly obstructive in nature.

We wish to express our gratitude to Col. Morrison and Col. Whalley for permission to carry on this investigation and publish this paper. Our thanks are also due to Lieut.-Col. McPherson, Major Kidson, Major Wilson, Major Shucksmith, Major Light, Capt. Oakes, Sister Bevan, and Sister Nicholson.

HUMAN-MILK INTOXICATION DUE TO B_1 AVITAMINOSIS

BY

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For the first few months after the birth of their infants the Chinese women in Hong Kong live in constant dread of losing them. This anxiety is comprehensible, taking into consideration the infantile mortality, which amounted to 345 per 1,000 live births in 1939 (Hong Kong Annual Medical Report)—i.e., more than one-third of all infants born alive died within their first year of life. A certain proportion of deaths occur suddenly in apparently healthy, well-fed, and well-cared-for babies, with a predilection for the male sex, thus giving rise to a belief among the Chinese that evil spirits, out of jealousy, snatch their infants, especially plump baby boys. Hence the rather pathetic efforts of the parents to protect their infants from such a fate: "joss" papers are pasted on the windows and "joss" sticks are burned before the entrance of their homes to prevent the incursion of evil spirits; the infants are disguised as animals by sewing fur ears on their caps; protective talismans are hung on their necks and chains on their ankles to fetter them, allegorically, to their homes. However, in spite of all these "precautions," a mother may find, to her horror, that her infant has died, unobserved, during the night or while strapped to her back (the usual method of carrying infants in China). Sometimes the mothers observe that their infants suddenly become cyanotic and dyspnoeic and die, apparently of suffocation. In such cases women believe that suffocation is due to "wind" which drives mucus into the child's throat. Furthermore, they believe that this "wind" is transmitted to the infants through their own milk, which is considered to be "no good."

Aetiology

Actually the belief that their milk is not good has been scientifically proved. In 1888 Hirota, in Tokyo, was the first to observe a complex of symptoms in infants fed by beriberic women, and he called this complex "infantile beriberi"—thus connecting this disease with a condition later found to be B_1 avitaminosis. Since then a number of Japanese workers (Ito, 1911; Asakura, 1932; Takamatsu, 1934), and also I myself (Fehily, 1940), have suggested that the milk of B_1-avitaminotic women, besides being vitamin-deficient, contains some toxic substance or substances. We now know that in B_1 avitaminosis, owing to a reduction of certain co-enzymes, the intermediary products of incomplete carbohydrate oxidation accumulate in the tissues, organs, and body fluids, including human milk. These intermediary metabolites are believed to consist of lactic acid, aceto-acetic acid, glycuronic acid, glyceraldehyde, acetaldehyde, dihydroxy-acetone, methylglyoxal, and others. Most of these intermediary metabolites (lactic acid excluded) are estimated as "bisulphite binding substances" (B.B.S.), which are found to be increased threefold to fourfold over normal values in all body fluids in B_1-avitaminotic living beings. After the administration of vitamin B_1 the B.B.S. decrease almost immediately to the normal values. Although the correlation between the intermediary metabolites and B_1 avitaminosis has been definitely established, many workers (Haynes and Weiss, 1940, and others) have proved that these metabolites are not the causative factor in the development of the acute nervous and cardiac symptoms encountered in this condition.

One of these substances—methylglyoxal—has been shown to be actively toxic (Kermak, Lambie, and Slatter, 1927; Vogt-Moller, 1931), and as it is never found in the milk of healthy women it has been suggested that this product is the toxic factor in the milk of B_1-avitaminotic women. However, various authors have stated (not in connexion with infantile beriberi) that other intermediary products, if in excess, are toxic, and this seems to have been demonstrated by many experiments, including the following (Haynes and Weiss, 1940):

> The administration of large doses of pyruvic acid or sodium pyruvate to normal and deficient rats was followed by death of the rats, both normal and deficient. Pyruvic acid in sublethal doses was especially irritating to the throat and had an injurious effect on the digestive and respiratory systems, whereas sodium pyruvate in sublethal doses produced diarrhoea. In the case of B_1-avitaminotic rats, the lethal dose of sodium pyruvate is smaller than that for normal rats, and the animals developed neurological symptoms shortly before death.

It would seem that the amount of pyruvic acid and sodium pyruvate in the milk of B_1-avitaminotic women is beyond the infantile tolerance, as one encounters all the above-mentioned symptoms as well as similar modes of death in infants fed on such a milk. It would seem also that besides methylglyoxal and pyruvates, other intermediary metabolites, in the amounts encountered in the milk, may take part in the intoxication, and their action would appear to be synergic and also cumulative, as even a few feeds may be fatal to an infant. This action is especially evident in acute cases, in which the intermediary metabolites may possibly give rise to acidosis similar to that of diabetic coma—an acute intoxication caused by the products of disordered carbohydrate and fat metabolism. In addition, it seems that the accumulation of intermediary metabolites alters the taste of the milk, as obviously hungry infants, after sucking greedily for a few moments, avert their heads protestingly and spill the milk (while water or cow's milk is taken without trouble).

Thus infantile beriberi differs considerably from the adult type, being primarily and mainly an intoxication, with acute

symptoms, short duration, and bad prognosis. Consequently the term "infantile beriberi" would seem to be misleading, and this may account for the non-recognition of the disease in some countries until comparatively recently. A more suitable term is therefore desirable; in 1911 Ito suggested that the disease be called "breast-milk intoxication," and recently I (Fehily, 1943) suggested the term "human-milk intoxication."

Symptoms

Although infants fed on the milk of B_1-avitaminotic women may present a characteristic habitus or acquire some persistent symptoms, the disease generally manifests itself in the form of attacks which develop shortly after breast-feeding. These attacks are characterized either by vomiting, abdominal pain (accompanied either by crying or by screaming), diarrhoea, and abdominal distension, or by vomiting, stiffness of the neck and extremities, and convulsions. In the most acute form the attack consists of dyspnoea, cyanosis, and running pulse. The attacks often end fatally, but in case of survival the infants pass into the chronic stage with symptoms of oedema, oliguria, aphonia, constipation, meteorism, neck retraction, enlargement of liver and right side of the heart, loss of weight, retarded growth, and marasmus. At the beginning of the intoxication the infants sometimes present a characteristic habitus: they are fat and flabby, pale and restless, and often have cough, which in some cases may be due to irritation by intermediary metabolites. The condition of the reflexes is variable, being normal, exaggerated, diminished, or absent. The temperature in uncomplicated cases is normal or subnormal. Probably as a result of the irritation and of the oedematous condition of the respiratory tract, intercurrent diseases, such as bronchitis and bronchopneumonia, are present in the majority of cases, and these complications contribute greatly to the extremely high mortality, which amounts in untreated cases to approximately 95%. Before the main cause of this high infantile mortality was recognized, in infant welfare centres in Hong Kong cod-liver oil, iron, and calcium mixtures were administered prophylactically as a routine, but without any noticeable effect on infantile morbidity or mortality.

The acuteness of milk intoxication is dependent on the amount of milk ingested; consequently overfed babies are more liable to acute attacks and to sudden death. These attacks, as well as other symptoms of the disease, disappear on the cessation of breast-feeding and its substitution even by foods such as diluted sweetened condensed milk or rice paste, which are deficient in vitamin B_1 and consist mainly of carbohydrates. With the resumption of breast-feeding the attacks reappear and eventually lead to death, unless the secretion of the mother's milk ceases or considerably diminishes. It would seem that infants born alive possess a reserve, however small, of vitamin B_1 and may progress satisfactorily until the accumulated intermediary products of carbohydrate metabolism are ingested in the milk of vitamin-B_1-deficient women. Thereafter the infants try to get rid of these intermediary metabolites by excretion through the kidneys (methylglyoxal can be found in the urine) and the lungs (the pungent smell of the breath often noted is probably due to pyruvic acid); but mainly by further oxidation of the metabolites to harmless end-products, provided sufficient vitamin B_1 is available. Consequently infants succumb to intoxication when their vitamin reserves become depleted. In infants born with a low vitamin reserve or those fed previously on vitamin-B_1-deficient food the intoxication is greatly accelerated. I observed the symptoms of acute milk intoxication in a 5-months-old poorly nourished infant, whose mother admitted, on close questioning, that until a week previously the child had been fed on sweetened condensed milk, she being a professional wet-nurse. (Incidentally during these five months she nursed two infants, both of whom succumbed to a disease similar to that of her own child.)

During the year 1939, of the infants brought to an infant welfare centre in Hong Kong, 18% showed manifest signs of milk intoxication; while 25% of the mothers complained of one or more of the following symptoms: weakness, numbness or oedema of the extremities, dyspnoea, palpitation, or meteorism (this latter condition often being an early sign of B_1 avitaminosis). The maternal beriberi and the milk intoxication in infants did not always correspond, owing to the fact that most of the women with manifest B_1 avitaminosis ceased to lactate, while those with good lactation were still in a latent stage.

Findings at Necropsy

In post-mortem examinations the most striking feature of human-milk intoxication (in uncomplicated cases) is the absence of any, or any significant, pathological lesions to account for death. The appearance of the infants, especially of those who died in an acute attack, is that of fat well-cared-for babies, sometimes cyanotic, but otherwise with normal organs and tissues. This absence of pathological lesions puzzled the medical profession in Hong Kong, and it was suggested that death might have been due to overlaying, to asphyxiation from charcoal fumes, or to accidental poisoning with native medicine. In some cases of milk intoxication oedema of the larynx was noted, in others hyperaemia of the intestines or enlargement of the right heart. In subacute cases one may find an internal anasarca—namely, oedema of the brain, respiratory tract, right heart (cause of its enlargement), spleen, liver, gall-bladder, and kidneys, as well as slight effusions into serous cavities. External oedema is comparatively rare, and if present is most likely to be seen in the form of a slight general puffiness or as a localized oedema—e.g., of the scrotum. This increased water retention may be due to acidosis (mainly lactic and pyruvic), as it has been pointed out (Fischer, 1921; Fliederbaum, 1932) that acidosis of tissues and organs increases their affinity for water. Death from human-milk intoxication, as in the acute cardiac beriberi of adults, is attributed to heart failure, caused through degeneration of the vagus nerve or loss of contractility of the heart muscle (owing to water retention). However, it is remarkable that no vagus degeneration has been reported in the case of infants who died of "infantile beriberi," and, furthermore, death may occur before the appearance of any pathological cardiac lesions, such as hydrops. It is also remarkable that cardiac stimulants do not produce any effect on the symptoms; whereas administration of vitamin B_1 is followed by a dramatic improvement and eventually by a *restitutio ad initio*. These facts would suggest that death may be of central origin (probably due to a biochemical lesion).

Since human-milk intoxication in infants is due to the ingestion of milk from B_1-avitaminotic women, one is inclined to seek an explanation for such widespread maternal B_1 avitaminosis.

Reason for Prevalence of Maternal B_1 Avitaminosis

It is generally accepted that the requirements of vitamin B_1 are in direct proportion to the intake of carbohydrates. In Hong Kong highly milled rice is the only staple food of the Chinese, and consequently B_1 avitaminosis is widespread. In the case of pregnant and lactating women this condition becomes aggravated and often manifests itself as beriberi, because of: (*a*) increased physiological requirements, (*b*) increased excretion of vitamin B_1 in milk, (*c*) increased appetite being satisfied mostly by highly milled rice, and (*d*) food prejudices. Thus they believe that fruit and vegetables are unhealthy because they give rise to "wind," which is transmitted with their milk to their infants. Consequently, they abstain from fruit and vegetables for at least one month after delivery—in the case of male infants often during the whole period of nursing. This custom, as well as the fact that male infants are often overfed, explains the apparent predilection of milk intoxication for the male sex.

From the beginning of the war large stocks of milled rice were stored in Hong Kong. Even highly milled rice, if fresh, contains a certain amount of vitamin B_1; but this gradually disappears on storage. In the course of time rice which had been stored for longer periods than hitherto was distributed to the population, with the result that B_1 avitaminosis, followed by pellagra and ariboflavinosis, increased tremendously and appeared even in institutions which up to then had been free of any deficiency diseases. Consequently, human-milk intoxication among infants must have correspondingly increased (no statistics are available). Indeed, one could see on the streets a greater number of infants with the characteristic habitus or the symptoms of chronic intoxication, or with the incipient cyanosis and dyspnoea of an acute attack. After the Japanese

occupation of the colony this long-stored rice was severely rationed, so that individuals received approximately only one-third of the amount previously consumed. Consequently undernourishment was added to B_1 avitaminosis, with the result that the secretion of lactating women either considerably diminished or completely ceased. Thereafter one could see many undernourished infants with the symptoms of chronic milk intoxication, while acute milk intoxication had apparently disappeared. It may seem incongruous, but the fact remains that a high incidence of acute human-milk intoxication in infants indicates a certain degree of prosperity in the case of the native population. The observations of Bray (1929) on the island of Nauru support this statement. There the natives were given royalties for their phosphate deposits. As a result there was a distinct drop in their production of native foods, which were replaced by imported white flour and tinned meat. As palm toddy was prohibited they consumed large quantities of sugar-water instead. This change of diet resulted in the appearance of acute human-milk intoxication, and the infantile mortality rate rose to 40%.

Human-milk intoxication occurs whenever the staple foods of women are vitamin-B_1-deficient carbohydrates. Admittedly, in Great Britain such staple foods as the national loaf and potatoes have enough vitamin B_1 for their own metabolism; however, if the bulk of the diet consists of carbohydrates, some of them refined, the balance may be upset and result in deficiencies. In fact, deficiencies of other components of the vitamin B complex—such, for example, as riboflavin and nicotinic acid—have been reported recently in England (Slater, 1942; Duckworth, 1942; Clarke and Prescott, 1943; and others).

An apparently healthy mother with latent B_1 avitaminosis may produce milk containing intermediary metabolites just above the infant's tolerance, which would lead to predisposition to infantile complaints such as respiratory infections or persistent intestinal catarrhs. Even before the war Geiger and Rosenberg (1933), in Palestine, reported that Jewish sucklings suffering from persistent diarrhoea with toxic symptoms and excreting methylglyoxal in the urine, were cured after the administration of vitamin B_1. Popoviciu and Munteanu (1934) observed similar gastro-intestinal disturbances in Rumanian infants, which they also attributed to deficiency of vitamin B_1 in human milk. Occasionally in the paediatric wards in continental Europe and in the United States of America one encounters cases of sudden death dyspnoea and cyanosis or learns of cases of sudden death in breast-fed infants. Where no pathological lesions are found to account for these occurrences, death is usually presumed to be due to status lymphaticus, laryngeal spasm, or oedema, to asphyxiation caused by blankets, pillows, or overlaying, or to strangulation with the strings of a jacket. May it not be possible that some, at least, of these puzzling and inadequately explained cases are due to human-milk intoxication?

Causes other than B_1 Avitaminosis

Furthermore, it is quite possible that accumulations of intermediary metabolites may also occur in other conditions in which there is a disordered carbohydrate metabolism, as in cases of glandular dysfunction—e.g., diabetes; or in other vitamin-deficiency diseases such as nicotinic acid and riboflavin deficiencies (the last two conditions most probably associated with B_1 avitaminosis).

It is conceivable that human milk intoxication occurs whenever B.B.S. are increased in the human body; and their increase has been found in various conditions other than B_1 avitaminosis—viz., acidosis, ketosis, anoxaemia, toxaemia, and uraemia (Wilkins, Taylor, and Weiss, 1937), as well as in diabetes, anaemia, epidemic dropsy, and splenomegaly (Wilson and Ghosh, 1937). However, the correlation between the nature and amount of intermediary metabolites in human milk and the symptoms in an infant fed on such a milk have yet to be definitely established. To the best of my knowledge such work has not yet been undertaken, my own investigations in that field having been curtailed after a short time.

It would seem that the statement that breast milk is the best food for an infant should be qualified by the proviso that it is secreted by a healthy woman.

Summary

It is suggested that the term "breast-milk intoxication" or "human-milk intoxication" be substituted for the term "infantile beriberi."

It is also suggested that in addition to methylglyoxal, hitherto considered to be the only toxic factor in the milk of B_1-avitaminotic women, other intermediary metabolites, in concentration encountered in the milk, may play an important part in human-milk intoxication.

The action of these intermediary metabolites appears to be synergic and cumulative.

The symptoms of human-milk intoxication are discussed.

It is pointed out that accumulation of intermediary metabolites in the milk of lactating women may be encountered in conditions other than B_1 avitaminosis and thus cause an intoxication.

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ACUTE BRACHIAL RADICULITIS

BY

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Spillane (1943) has drawn attention to the comparative frequency of cases of neuritis of the nerves around the shoulder girdle in his experience with the M.E.F. Cases also occur in which the incidence is predominantly on the roots of the brachial plexus rather than on the peripheral nerves, and combinations of these conditions are seen in other patients. This paper is based on 36 cases—24 personally observed in various stages of the disease and 12 seen by Major Philip Buckley, R.A.M.C.

The essential clinical picture is a simple one: severe pain starts across the back of the shoulder and radiates down the outer side of the arm and sometimes on to the upper part of the chest; the pain remains severe for a few days and then weakness of the shoulder develops, sometimes accompanied by numbness. As the paralysis appears the severe pain usually passes off and is replaced by a dull ache, the paralysis persisting.

Illustrative Case History

An R.A.F. corporal aged 33 was admitted to hospital on Sept. 15, 1942, with the history that six weeks previously he had developed very severe pain across the back of both shoulder-blades, which radiated down the outer side of the right arm and forearm; the severe pain persisted for about five days and was then replaced by a dull ache. On the third day of the severe pain he noted considerable weakness of both arms, but especially the right, and this weakness had persisted unchanged. There were no general symptoms of malaise or fever at the onset of the illness, and his past history was uneventful except for attacks of migraine.

On examination he had winging of the left scapula due to paralysis of the serratus magnus. In the right arm there was considerable wasting of the spinati, deltoid, biceps, supinator longus, and the clavicular head of the pectoralis major. There was minimal voluntary power in the supinator longus, while the other wasted muscles were weak; the biceps and supinator jerks were absent, and the triceps jerk just present. On sensory testing there was impairment of cutaneous sensibility down the outer side of the right arm